

ABSTRACT

PURIFICATION METHODS FOR OLIGONUCLEOTIDES AND THEIR ANALOGS

The present invention discloses methods for separating oligonucleotides from impurities. In the methods of the invention, a target oligonucleotide, in a mixture comprising the target oligonucleotide and an impurity, is separated from the impurity using a titratable anion exchange composition. The target oligonucleotide is bound to the titratable anion exchange composition and an eluting solution which increases in pH over time is passed through the titratable anion exchange composition with the target oligonucleotide bound. Preferably, the eluting solution does not substantially increase its salt concentration. The target oligonucleotide is eluted and separated from the impurity which either elutes at a lower pH or a higher pH than the target oligonucleotide.